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Title

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Abstract

Impairments in classical fear conditioning and deficits in discriminative learning are observed in posttraumatic stress disorder (PTSD). However, it is unknown whether similar impairments can be found with types of discriminative learning other than classical conditioning, such as evaluative conditioning (EC), in which the valence of a stimulus can be transferred to other stimuli. In this study, we investigated whether EC is also influenced by traumatic experiences independently of presence of PTSD. We tested 14 accident survivors with remitted PTSD, 14 survivors without PTSD, and 16 non-trauma controls. We used behavioral measures, psychophysiological indicators, and subjective ratings for tasks. General effects of learning were observed across groups and conditioning/extinction. Trauma controls had slower reaction times (RTs) to the aversive conditioned stimulus compared to appetitive conditioned and neutral stimuli, as well as slower RTs and increased accuracy during conditioning than during extinction. Remitted PTSD participants showed opposite results, demonstrating decreased accuracy and slower RTs during conditioning as compared to during extinction. No discriminative effect was found in the non-trauma controls and the remitted PTSD participants. These results suggest that a traumatic experience influences EC, and that this influence differs between individuals who have and have not developed PTSD after traumatic exposure.

Keywords

discriminative conditioning, evaluative conditioning, trauma, psychophysiology, posttraumatic stress disorder (PTSD), learning

1. Introduction

Posttraumatic stress disorder (PTSD) is a severe mental disorder, characterized by intrusion, avoidance, negative alterations in cognitions and mood, and alterations in arousal and reactivity following exposure to traumatic events (American Psychiatric Association, 2013). The lifetime prevalence of PTSD in the general adult population of the United States is 6.8% (Kessler et al., 2005). PTSD was reclassified in the DSM-5 as a trauma- and stressor-related disorder (American Psychiatric Association, 2013).

Our understanding of the development and maintenance of PTSD has greatly improved by advances in the analysis of associative learning mechanisms, such as classical fear conditioning (LeDoux, 2014; Pitman et al., 2012; Yehuda and LeDoux, 2007). Trauma survivors react to a traumatic event (unconditioned stimulus; US) with a fear response (unconditioned response; UCR). Individuals who develop PTSD in the aftermath of the traumatic event continue to show a fear response (conditioned response; CR) when confronted with trauma-related cues (conditioned stimulus; CS), long after the trauma (Yehuda and LeDoux, 2007). In several studies, using discriminative fear learning procedures in which one CS predicts the immediate occurrence of an aversive event (CS+) and another predicts the non-occurrence of this event (CS-), PTSD participants showed enhanced conditioned responses during acquisition (Norrholm et al., 2011; Orr et al., 2000; Peri et al., 2000; Wessa and Flor, 2007), lack of differential responses (Grillon and Morgan, 1999), deficits in fear inhibition by a safety signal (Jovanovic et al., 2010; Jovanovic et al., 2009; Jovanovic et al., 2013; Sijbrandij et al., 2013), and impairment in extinction (Blechert et al., 2007; Milad et al., 2009; Orr et al., 2000; Peri et al., 2000; Wessa and Flor, 2007). However, it is not clear whether impairment in discriminative learning is specific for classical fear conditioning or can also be found in other forms of discriminative conditioning, such as evaluative conditioning (EC) (Figure 1).

EC is the process by which the valence of a stimulus (positive, negative, or neutral) can be transferred to other stimuli when they are repeatedly presented together (De Houwer et al., 2001; Hofmann et al., 2010; Martin-Soelch et al., 2007). The potential difference between classical conditioning and EC resides in the nature of the US. In the fear conditioning paradigm, an aversive stimulus (e.g., cutaneous shock) elicits a physiological reflex, whereas in EC, the US (e.g., perceived financial loss) is characterized by its valence (Martin-Soelch et al., 2007). In the psychopathological aspects, EC was used already to understand fear and disgust responses (Woody and Teachman, 2000) in healthy participants (Engelhard et al., 2014; Olatunji et al., 2007) and in patients with specific phobia (Olatunji et al., 2009). As we searched the literature, we did not find any studies that investigated EC in patients with PTSD or trauma survivors. The results of a study with 122 healthy volunteers showed an EC effect in that participants disliked neutral objects preceding traumatic pictures more than neutral stimuli preceding neutral pictures (Ehlers et al., 2012).

However, it is not clear whether the impairments in EC are observed in PTSD patients, and whether they are a consequence of experiencing a trauma rather than a characteristic of PTSD symptoms. Here we examined severely injured accident survivors with subsequent PTSD that had remitted at the time of the study (remitted PTSD), accident survivors who had not developed PTSD (trauma controls), and subjects who had never experienced a trauma (non-trauma controls). Our aim was to investigate the effect of a traumatic experience with and without the transient manifestation of

PTSD on discriminative conditioning, and particularly, on EC. Assuming an effect of trauma on learning processes (Yehuda and LeDoux, 2007), we expected impaired EC in subjects with remitted PTSD and trauma controls, but not in non-trauma controls. We additionally expected stronger learning effects to aversive stimuli and weaker learning effects associated with the CS- in the remitted PTSD group as compared to resilient individuals (trauma controls).

2. Methods

2.1 Participants

Twenty-two accident survivors with remitted PTSD and 18 resilient accident survivors who had not developed PTSD were recruited from two samples of physically injured subjects. All subjects had been hospitalized at the Department of Traumatology at the University Hospital Zurich 10 years ago and had taken part in earlier studies looking into the psychosocial consequences of accidental injuries (Schnyder et al., 2001; Schnyder et al., 2008). We contacted the 456 participants of the earlier studies, from which 113 had been diagnosed with PTSD after the accident. From these samples, 25 individuals who had received a PTSD diagnosis after the accident and 20 individuals without PTSD diagnosis were interested to participate in the current study. Among the 25 participants who had received a PTSD diagnosis, 3 had currently PTSD symptoms; and were therefore excluded from the remitted group. The number of individuals with current PTSD symptoms was however too small to be analyzed as a separate group. Only 20 participants from the 343 resilient participants were interested in participating in the current study. From these 20 participants, 18 fulfilled the inclusion criteria after screening and could be enrolled in the current study.

At the time of the accident, a Glasgow Coma Scale (GCS) (Teasdale and Jennett, 1974) score of 9 or more had been required for inclusion, thus excluding all patients with severe head injuries. Although GCS scores were 15 (indicating fully awake) in all participants of this study, five participants in the PTSD-remitted group and one in the trauma-control group had been clinically diagnosed with mild traumatic brain injury (TBI) according to the medical records. The severity of injuries was assessed by the Injury Severity Scale (ISS) (Baker and O'Neill, 1976). Mean scores on ISS were 17.79 (range 4-41) in the PTSD-remitted group and 10.07 (range 4-34) in the trauma-control group. Two-sample t-test revealed that there was a significant difference between two groups ($t(26) = 2.15$, $p = 0.04$). These patients had initially received a thorough psychiatric diagnostic assessment shortly after the accident, and again at 6 months and 12 months post-trauma (Schnyder et al., 2001). For the non-trauma group, 16 healthy controls with matched age and gender were recruited from the general population through advertisements (non-trauma group). All subjects were over 18 years of age. To be included in the PTSD-remitted group, subjects had to have been diagnosed with full or subsyndromal PTSD according to the DSM-IV, as assessed by the German version (Schnyder and Moergeli, 2002) of the Clinician-Administered PTSD Scale (CAPS) (Blake et al., 1995) at least at one of the measurement points in the previous studies (full PTSD: fulfilling symptom clusters A, B, C and D; subsyndromal PTSD: fulfilling symptom clusters A, B plus either C or D but not both), but not in the present study. For participants to be included in the trauma-control group, they were required to never have had a diagnosis of full or subsyndromal PTSD during the previous studies. Inclusion criteria for the non-trauma group were that the participants had never experienced a potentially traumatic event according to DSM-IV PTSD criterion A. Exclusion criteria for all three groups were current mental disorders, chronic somatic and neurological diseases, and insufficient command of the German language. Participants were thoroughly informed about the procedures and gave written informed consent according to the Declaration of Helsinki before participating. Ethical approval was granted by the ethics committee of the canton of Zurich, Switzerland.

In total, eight participants from the remitted PTSD group and four participants from the trauma-controls were excluded from the study. Seven participants were excluded due to current PTSD, current major depression, anxiety disorders, chronic somatic disease or chronic pain. One participant was excluded because of insufficient understanding of the experiment. For one participant the CAPS was missing, and for another the question about how long they were free from symptoms was missing. We could not obtain any data of one participant due to technical problems and because this participant had answered the questions even before having read them. For three subjects, we could not obtain the whole (n=1) or partial (n=2) physiological data because of technical problems. In regard to partial data losses due to technical problems, one participant out of two lacked the data of the second phase of conditioning and extinction; the other person lacked the data of the second phase of extinction. The description of the final sample (n=44) is given in Table 1.

2.2. Psychometrics

Current PTSD symptoms were assessed using the German version (Schnyder and Moergeli, 2002) of the Clinician-Administered PTSD Scale (CAPS)(Blake et al., 1995). Axis I comorbidity was established by the Mini International Neuropsychiatric Interview (M.I.N.I.) (Sheehan et al., 1998). Symptoms of depression were measured by the German version (Hautzinger et al., 1995) of the Beck Depression Inventory (BDI) (Beck et al., 1961) and trait anxiety by the German version of the State Trait Anxiety Inventory (STAI) (Laux et al., 1981). The absence of traumatic events in the non-trauma group was verified by the German version of the first part of the Posttraumatic Stress Diagnostic Scale (PDS) (Foa et al., 1997). We measured verbal intelligence using the "Wortschatztest" (WST; (Schmidt and Metzler, 1992)), a multiple choice word comprehension test that is a German equivalent to the "Spot-The-Word" test (Baddeley et al., 1993).

2.3. Physiological measures

Physiological data was collected with the BIOPAC MP150 System (Biopac Systems, Inc., Goleta, CA). Electrocardiograms (ECG) were recorded with 3 Ag/AgCl disposable snap connector electrodes filled with hydrogel jelly located below the left and right collarbone and on the left rib cage. Skin conductance electrodes were placed on the thenar and hypothenar eminence of the left palmar surface using Ag-AgCl electrodes filled with isotonic electrolyte jelly. These methods were used in a previously published study (Schumacher et al., 2013).

2.4. Data reduction (physiology)

Autonomic Nervous System Laboratory 2.51 (ANSLAB; Wilhelm, F. H. & Peyk, P., 2005; available at the SPR Software Repository: http://www.sprweb.org) was used to filter the raw data, to correct for artifacts, and to extract mean and maximum scores for event and baseline intervals. The ECG signal was 0.5-40Hz band-pass and 50Hz notch filtered. Skin conductance was 1Hz low-pass filtered. Heart rate (HR) was converted from the inter-beat interval. HR responses were calculated by subtracting the mean value during the 2s baseline interval prior to the onset of the stimulus from the mean value during the 6s interval following stimulus onset. For skin conductance (SC) responses, the mean value during the 2s baseline interval was subtracted from the maximum value during the 6s interval following stimulus onset.

2.5. Discriminative conditioning task

We used an EC (appetitive and aversive) procedure that has been developed and validated by our group (Martin-Soelch et al., 2006; Muheim, 2005). The currency rewarded during the experiment was in Swiss Francs (CHF). One, two or three pieces of apples (CS+pos) were presented and immediately followed by the presentation of a CHF 1 coin (US) indicating the win of CHF 1, grapes (CS+neg) by a crossed out CHF

0.5 coin (US) indicating the loss of CHF 0.5, and cherries (CS-) by a blank screen (neutral condition; Figure 2). After a 1500ms delay, the current account balance was displayed on the screen. Subjects had to indicate how many pieces of fruits were displayed. The association between CS and US was independent of responses. We used a 50% partial reinforcement strategy, in which only half of the presentations of the CS+ were paired with the US. In order to control for habituation effect, the stimuli used in the conditioning experiment were presented 5 times in a randomized order to the participants before conditioning. The conditioning trials lasted for about 10 minutes and were followed by extinction trials, in which the same fruit pictures were displayed, but no longer followed by monetary gain or loss. Subjects rated each of the presented stimuli (CSs and USs) for valence, arousal, and expectation of win or loss before and after conditioning, and after extinction; a 1-to-100 point visual analogue scale (VAS) was used for ratings. Subjects were instructed that they would perform a time-sensitive reaction task, in which they could win money in a randomized way, and that they would receive the amount of cash displayed at the end of the experiment. They were not aware of the conditioning process and were not informed about the association between CS and US until the end of the experiment. In EC studies, it is relatively common to use cover stories to reduce the likelihood of demand awareness (De Houwer et al., 2001; Hofmann et al., 2010). Reaction time (RT) to the CSs was measured as a behavioral indicator of learning (Craddock et al., 2012; Dawson et al., 1982; Lissek et al., 2008). The total amount of money that could be won was CHF 15 in addition to a fixed monetary compensation for participating in the study. The experiment was programmed in such a way that all participants won the same amount of money at the end. In a pilot study with 42 healthy individuals, significantly different patterns were observed by valence, arousal, and expectation among CS-, CS+pos, and CS+neg. The reaction times were also different between the CS types following conditioning (Muheim, 2005).

2.6. Data analysis

Statistical analyses were performed using IBM SPSS Statistics 22 (IBM Corp., Armonk, NY, USA). We used a linear mixed models design and applied restricted maximum likelihood estimation to compare conditions. Full-factorial models were calculated separately for physiological (HR and SC responses) and behavioral (RTs, accuracy, picture valence ratings, picture arousal ratings, picture expectation ratings) measures. For each CS-type (CS+pos, CS+neg, CS-), we divided the trials presented during each condition (conditioning, extinction) into 3 blocks of equal numbers of trials to assess the changes over time during each condition. Group (subjects with remitted

PTSD, trauma controls, non-trauma controls), condition, and CS-type were treated as fixed effects in models for RT, accuracy, HR and SC responses. Group, time (before conditioning, after conditioning, after extinction), and CS-type were treated as fixed effects in models for picture ratings. In all models, subjects were treated as a random effect. Models were optimized by selecting a covariance structure for the repeated observations which produced the lowest Akaike's Information Criterion (AIC). A first order ante-dependent structure was fitted for picture and mood ratings, a heterogenous first-order autoregressive structure for RTs and accuracy, a first-order anti-dependent structure for SC responses, and a heterogeneous first-order factor analytic structure for HR responses. Bonferroni corrected pairwise comparisons based on the estimated marginal means were used as post-hoc tests.

3. Results

3.1. Reaction time

We found interaction effects of group x condition (F (2, 746.3) = 11.3, $p <$ 0.001) and group x CS-type (F (4, 1759.1) = 2.4, $p = 0.045$) on RT. As shown in Figure 3 (upper row), remitted PTSD subjects responded slower during conditioning than during extinction (mean difference =54.34, 95% CI [23.55, 85.13]) while trauma controls responded faster during conditioning than during extinction (mean difference = -45.40 ms, 95% CI [-76.08, -14.72]). Response speed of non-trauma controls was similar during conditioning and extinction ($p = 0.123$). As shown in Figure 3 (lower row) trauma controls responded slower to CS+neg than to CS+pos (mean difference = 40.38 ms, 95% CI [4.67, 76.10]) and CS- (mean difference = 71.63 ms, 95% CI [36.18, 107.07]) across conditions. Response speed was not significantly different between CS-types for remitted PTSD patients ($ps \geq 0.273$) or non-trauma controls ($ps \geq 0.200$).

3.2. Accuracy

We found an interaction effect of group x condition (F(2, 190.4) = 3.3, p = 0.037) for accuracy (Figure 3, upper row). In trauma controls the percentage of correct responses was higher during conditioning than during extinction (mean difference = 3.04%, 95% CI [0.47, 5.62]) while there was no significant difference in accuracy between conditions for the other groups ($ps \geq 0.257$). During extinction, the percentage of correct responses was lower for trauma controls than non-trauma controls (mean difference = -5.32%, 95% CI [-9.69, -0.95]).

3.3 Physiology

Main effects of condition (F (1, 724.0) = 25.72, p < 0.001) and CS-type (F (2, 1217.0) = 5.10, p = 0.006) were found for SC responses. SC responses were larger during conditioning than during extinction (mean difference = 0.09 μS, 95% CI [0.05, 0.12]). SC responses to CS+pos were smaller than to CS+neg (mean difference = -0.05 μS, 95% CI [-0.10, -0.01]) and CS- (mean difference = -0.05 μS, 95% CI [-0.09, -0.01]) across conditions.

A main effect of CS-block (F(2, 1384.7) = 3.30, p = 0.037) was found for HR. Pairwise comparisons for CS-block revealed no significant effects.

3.4. Ratings

There was a group x condition interaction on picture expectation ratings (F(4, 73.9) = 3.36, p = 0.014). Across stimuli, trauma controls showed more positive expectations before conditioning than after extinction (mean difference = 11.07, 95% CI [2.68, 19.46]). All other pairwise comparisons were not significant (ps > 0.2).

For picture valence ratings, significant main effects of condition (F(2, 51.2) = 4.12, p = 0.022) and CS-type (F(2, 104.4) = 3.61, p = 0.031) were found. Across groups, pictures were more positively rated before conditioning than after extinction (mean difference = 7.87, 95% CI [1.14, 14.61]). Across groups and conditions, CS- was significantly more positively rated than CS+pos (mean difference = 4.67, 95% CI [0.03, 9.31]). No significant main or interaction effects of group, condition, or CS-type were found for picture arousal ratings (ps > 0.1).

3.5 Contingency awareness

About a third of the participants (n=16; 36.4%) answered that they had recognized contingency between CS and US. There were no significant differences between groups ($\chi 2$ (2) = 2.646, p = 0.299).

4. Discussion

Our study investigated discriminative evaluative conditioning in trauma survivors. We expected the experience of trauma to affect EC, independent of PTSD symptoms. Our results only partially confirmed this hypothesis. We found general effects of learning across groups and conditioning/extinction on RTs and SC responses, but also specific discriminative learning patterns in the three groups of participants. More specifically, the group of trauma controls showed changes related to discriminative learning and to conditioning versus extinction mostly at the behavioral level. The remitted PTSD participants showed changes in the behavioral reactions (i.e., RTs) during conditioning and extinction that were opposite to the ones evidenced in the trauma-control group.

General learning effects included significantly faster RTs to the CS- (the neutral condition), than to both CS+ (negative and positive), which was accompanied by a more positive rating. RTs were significantly faster during the middle and end phases than during the first phase of the conditioning trials; RTs were also faster at the end of the conditioning phase than at the end of the extinction phase. Specific learning effects from the middle phase of the tasks are also reflected by the significantly higher percentage of correct responses during the middle and the end of the tasks compared to the beginning across conditions; this is also evident by differential SC responses to the different CSs during the middle and end phases of the conditioning and extinction tasks, but not at the beginning. SC responses were significantly larger for CS+neg and CS- than for CS+pos. Some findings differentiated between the conditioning and extinction tasks, including faster RTs at the end of the conditioning compared to the end of the extinction tasks, and larger SC responses during conditioning than during extinction. This suggests that the learning processes were different during conditioning and extinction.

RTs have been used as a reliable index of conditioning (Craddock et al., 2012; Dawson et al., 1982; Lissek et al., 2008). As expected, in our study we found temporal learning effects for the RTs as the differences between the CS types appeared within the middle phase of conditioning and extinction. This is in line with previous studies on the differential learning effects, which were expressed by faster RTs to CS- than to CS+ during classical conditioning (Dawson et al., 1982; Hermans et al., 2005; Lipp et al., 1993). However, studies on the olfactory discriminative learning showed a faster response in CS+aversive and CS+appetitive than CS- in the first half of the conditioning (Gottfried and Dolan, 2004; Gottfried et al., 2002).

The observed faster RTs to CS- during learning in our sample could be explained by the underlying group differences. Specifically, the group of trauma-controls evidenced slower RTs to the aversive CS+ compared to the CS- and the appetitive CS+. Non-trauma controls as well as remitted PTSD participants did not show any RT differences between the CS types. Further, trauma-controls evidenced learning responses distinguishing conditioning and extinction, expressed by faster RTs during conditioning than during extinction. The remitted PTSD individuals showed an opposite pattern of changes in RTs, with slower RTs during conditioning than extinction. This could be a first indication that differential learning specifically took place in the group of non-trauma controls only. This hypothesis is further supported by the results related to accuracy.

We found specific learning effects for the trauma controls, who showed more correct responses during conditioning than during extinction. Trauma controls also showed less correct responses during extinction than non-trauma controls. Additionally, trauma-controls developed changes in the expectation related to the stimuli, with more positive expectation before conditioning than after extinction.

The group differences observed for our behavioral measures, i.e. RTs and accuracy are not in line with our hypothesis and suggest that in both groups exposed to trauma, trauma-controls show differential learning patterns related to EC. The faster RTs in association with the better accuracy during conditioning that we observed in the trauma-controls suggest that these individuals specifically manifest learning effects during conditioning that disappeared during extinction. The opposite reaction in the remitted PTSD group suggests that these functional learning responses are impaired in this group, which would be in line with results showing deficits in discriminative learning and extinction in individuals with PTSD (Grillon and Morgan, 1999; Milad et al., 2009). Therefore, it can be hypothesized that at the behavioral level, the remitted PTSD individuals have more similar reactions to individuals with current PTSD than to trauma-controls.

At the physiological level, we observed evidence for learning effects on SC responses, including larger responses during conditioning than during extinction and smaller responses to CS+pos than to CS+neg and to CS- that appeared during the course of the experiment. However, these changes were not different between the groups, and were in line with the RT results. They are also not in line with previous results showing differential SC responses during conditioning of appetitive and aversive odors (Hermann et al., 2000). Low contingency awareness of our study might affect differential SC responses; a study demonstrated that differential SC were not found in the 50% contingency group (Schultz and Helmstetter, 2010).

Taken together, these findings suggest that the main differences between our groups are found between the remitted PTSD and the two other groups, rather than between trauma-exposed participants and non-trauma exposed participants. Remitted PTSD participants differed from the trauma-control group mainly in the changes in RTs between conditioning and extinction. This could be related to impaired discriminative function and extinction processes also reported in individuals currently suffering from PTSD (Yehuda and LeDoux, 2007).

Several limitations require consideration. Our cross-sectional study design could not explain any causality. Because of a lack of current PTSD group, we could not obtain data about the relationship between EC and current PTSD symptomatology. In addition, we had no information on the learning function of the remitted PTSD individuals while they were suffering PTSD symptoms.The sample size was small and the results remain exploratory. The differences of verbal IQ and ISS among the groups might have an effect on the outcomes. The presentation of the conditioning and extinction phases within minutes of each other might have mixed habituation components with the extinction process. This procedure is however not uncommon in conditioning experiments in human (Baeyens et al., 1989). The results might be influenced by the contingency awareness during the experiment. The literature on contingency awareness shows inconsistent findings (De Houwer et al., 2001; Hofmann et al., 2010), with some studies reporting EC effects when participants were not aware of the CS-US contingencies (Baeyens et al., 1993; Balas and Sweklej, 2012) whereas others report that EC occurs only after the participants become aware of the contingency between the CS and the US with which it was paired (Pleyers et al., 2007). In our study, however, a large majority of the participants were not aware of the contingency but we still observed behavioral and physiological changes related to learning.

In conclusion, our preliminary study suggests that deficiencies in discriminative learning can be found in remitted PTSD patients at a time as temporally remote as 10 years after trauma. Additionally, we demonstrated effects of trauma on EC that were specific to the remitted PTSD individuals and could not be found in the resilient group of trauma controls. To our knowledge, this is the first study investigating the effect of traumatic experiences on EC. Our findings suggest that impairment in discriminative fear conditioning observed in traumatized participants can be extended to other forms of discriminative learning, such as EC. Further studies are needed in order to confirm the longitudinal influences of EC on accident survivors as well as survivors of other types of potentially traumatic events.

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Captions for figures

Figure 1: Illustration of conditioning procedures

A. Classical and evaluative conditioning:

In classical conditioning, the repeated association of a neutral stimulus (NS) with an unconditioned stimulus (US) will produce the same reaction to the NS as to the US. The unconditioned reaction (UR) that was produced by the US is elicited by the NS after the conditioning process and is called conditioned reaction (CR). In evaluative conditioning, the valence of an unconditioned stimulus (US), described as unconditioned valence (UV) in the figure, can be transferred to a neutral stimulus (NS), when it is repeatedly presented together with the US. The NS is then associated with the valence of the US and becomes a conditioned stimulus (CS) with a conditioned valence (CV).

B. Discriminative conditioning: In discriminative learning, the occurrence of a specific stimulus, the CS+, predicts the immediate occurrence of a positive or negative event, i.e., the US, which is in turn associated with an unconditioned response (UR) and another stimulus, the CS-, predicts the non-occurrence of this event. After conditioning, the CS+ can elicit the same reaction as the US, now called the conditioned reaction (CR), while the CS- does not elicit this response. Discriminative conditioning can be used in all forms of conditioning, e.g. here for classical and evaluative conditioning.

Figure adapted from Martin-Soelch, Linthicum & Ernst (2007). Reproduced with permission.

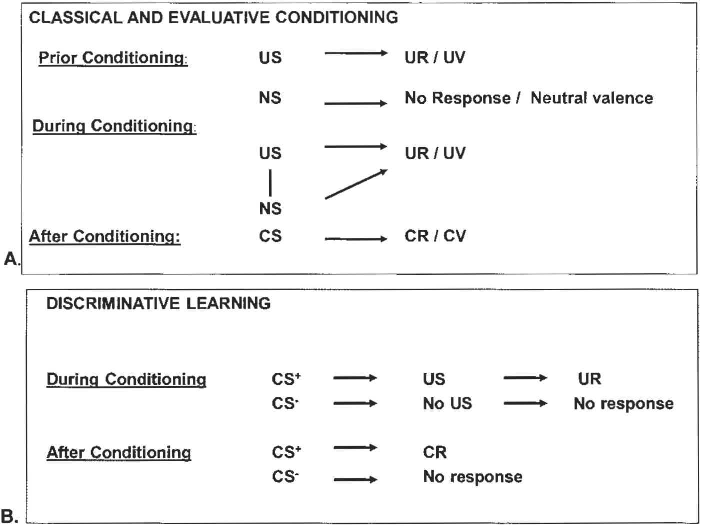

CLASSICAL AND EVALUATIVE CONDITIONING
Prior Conditioning:
US
UR / UV
NS
No Response / Neutral valence
During Conditioning:
US
UR / UV
NS
After Conditioning:
CS
CR / CV
A.
DISCRIMINATIVE LEARNING
During Conditioning
CS+
US
UR
CS-
No US
No response
After Conditioning
CS+
CR
CS-
No response
B.

Figure 2: Graphical representation of the trials for the appetitive CS+ (CS+pos), the aversive CS+ (CS+neg) and the neutral CS (CS-); ISI: interstimulus interval

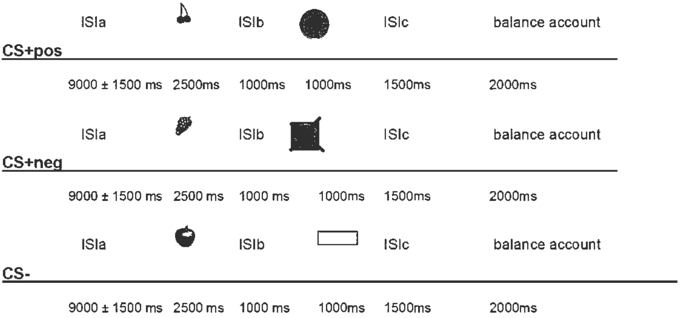
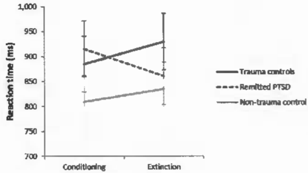
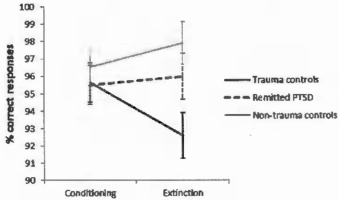

ISIa
ISIb
ISIc
balance account
CS+pos
9000 ± 1500 ms
2500ms
1000ms
1000ms
1500ms
2000ms
ISIa
ISIb
ISIc
balance account
CS+neg
9000 ± 1500 ms
2500 ms
1000 ms
1000ms
1500ms
2000ms
ISIa
ISIb
ISIc
balance account
CS-
9000 ± 1500 ms
2500 ms
1000 ms
1000ms
1500ms
2000ms

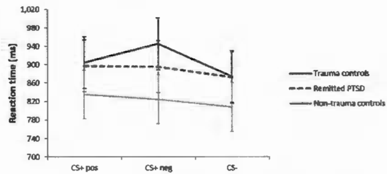
Figure 3. Reaction time and accuracy in subjects with remitted PTSD, trauma controls, and non-trauma controls by condition (upper row) and CS-type (lower row).



1,000
950
900
850
800
750
700
Reaction time (ms)
Conditioning
Extinction
Trauma controls
Remitted PTSD
Non-trauma control



100
99
98
97
96
95
94
93
92
91
90
% correct responses
Conditioning
Extinction
Trauma controls
Remitted PTSD
Non-trauma controls



1,020
980
940
900
860
820
780
740
700
Reaction time (ms)
CS+ pos
CS+ neg
CS-
Trauma controls
Remitted PTSD
Non-trauma controls

Table 1. Sample description

	PTSD-remitted (n = 14)		Trauma controls (n = 14)		Non-trauma controls (n = 16)				
	n	%	n	%	n	%	Chi^2	df	p
Women	9	64.3	8	57.1	10	62.5	0.16	2	0.921
	M	SD	M	SD	M	SD	F	df	p
Age	54.2	9.8	58.6	7.1	54.1	10.3	1.14	2, 41	0.329
Years of education	13.4	2.8	13.9	2.2	15.1	3.9	1.25	2, 41	0.296
STAI - trait anxiety	34.1	4.4	31.7	4.6	35.5	6.6	1.88	2, 41	0.165
BDI - depression	7.2	3.5	5.4	4.1	5.2	4.5	1.07	2, 41	0.353
Verbal IQ*	103.1	11.8	112.9	9.7	112.7	12.5	3.4	2, 41	0.043
	M	SD	M	SD	M	SD	t	df	p
CAPS – current total score	6.4	7.9	2.4	3.9			-1.67	25	0.107
Years since trauma exposure	11.4	1.8	9.9	0.4			-3.14	14.1	0.007
No. of traumata before accident	0.57	0.85	0.36	0.63			-0.76	26	0.457
No. of traumata after accident	1.5	1.56	1.21	1.19			-0.55	26	0.590
Years without symptoms	7.4	5.0							

Notes. STAI: the State Trait Anxiety Inventory, BDI: the Beck Depression Inventory, CAPS: the Clinician-Administered PTSD Scale.

* post-hoc pairwise comparisons: p values > 0.085, contrast PTSD-remitted vs. all other participants: t = 2.60, df = 41, p = 0.013

The authors report nu financial or other relations relevant to the subject of this article.

Contributors

M. Oe conducted the literature review, and wrote the first draft of the manuscript. S. Schumacher supervised the data collection, and conducted statistical analysis and edited the manuscript. U. Schnyder designed the study, supervised the patient's recruitment and edited the manuscript. C. Mueller-Pfeiffer designed the study, supervised the patient's recruitment and edited the manuscript. F. H. Wilhelm designed the study, supervised the analysis of physiological data and edited the manuscript. E. Kuelen collected data and wrote a preliminary draft of the manuscript. C. Martin-Soelch designed the study, supervised the data collection, the participants' recruitment, and the statistical analysis, and edited the manuscript. All authors contributed to and have approved the final manuscript.